

Chapter 230

Tests for Two Proportions in a Cluster-Randomized Design

Introduction

A *cluster (group) randomized design* is one in which whole units, or clusters, of subjects are randomized to the groups rather than the individual subjects in those clusters. However, the conclusions of the study concern individual subjects rather than the clusters. Examples of clusters are families, school classes, neighborhoods, and hospital wards.

Cluster-randomized designs are often adopted when there is a high risk of contamination if cluster members were randomized individually. For example, it may be difficult for an instructor to use two methods of teaching individuals in the same class. The price of randomizing by clusters is a loss of efficiency--the number of subjects needed to obtain a certain level of precision in a cluster-randomized trial is usually much larger than the number needed when the subjects are randomized individually. Hence, the standard methods of sample size estimation cannot be used.

Technical Details

Our formulation comes from Donner and Klar (2000). Denote a binary observation by Y_{gkm} where $g = 1$ or 2 is the group, $k = 1, 2, \dots, K_g$ is a cluster within group g , and $m = 1, 2, \dots, M_g$ is an individual in cluster k of group g . The results that follow assume an equal number of individuals per cluster. When the number of subjects from cluster to cluster are about the same, the power and sample size values should be fairly accurate. In these cases, the average number of subjects per cluster can be used.

The statistical hypothesis that is tested concerns the difference between the two group proportions, p_1 and p_2 . When necessary, we assume that group 1 is the treatment group and group 2 is the control group. With a simple modification, all of the large-sample sample size formulas that are listed in the module for testing two proportions can be used here.

When the individual subjects are randomly assigned to one of the two groups, the variance of the sample proportion is

$$\sigma_{S,g}^2 = \frac{p_g(1-p_g)}{n_g}$$

When the randomization is by clusters of subjects, the variance of the sample proportion is

$$\begin{aligned}\sigma_{C,g}^2 &= \frac{p_g(1-p_g)(1+(m_g-1)\rho)}{k_g m_g} \\ &= \sigma_{S,g}^2 [1+(m_g-1)\rho] \\ &= F_{g,\rho} \sigma_{S,g}^2\end{aligned}$$

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The factor $[1 + (m_g - 1)\rho]$ is called the *inflation factor*. The Greek letter ρ is used to represent the *intracluster correlation coefficient (ICC)*. This correlation may be thought of as the simple correlation between any two subjects within the same cluster. If we stipulate that ρ is positive, it may also be interpreted as the proportion of total variability that is attributable to differences between clusters. This value is critical to the sample size calculation.

The asymptotic formulas that were used in comparing two proportions (see Chapter 200, "Tests for Two Proportions") may be used with cluster-randomized designs as well, as long as an adjustment is made for the inflation factor. The basic form of the z-test becomes

$$z = \frac{|\hat{D} - \delta_0|}{\hat{\sigma}_{\hat{D}}(\delta_0)}$$

where

$$\hat{D} = \hat{p}_1 - \hat{p}_2$$

$$\delta_0 = p_1 - p_2 | H_0$$

$$\hat{\sigma}_{\hat{D}}(\delta_0) = \sqrt{\frac{\tilde{p}_1(1 - \tilde{p}_1)F_{1,\rho}}{n_1} + \frac{\tilde{p}_2(1 - \tilde{p}_2)F_{2,\rho}}{n_2}}$$

The quantities \tilde{p}_1 and \tilde{p}_2 are the maximum likelihood estimates constrained by $\tilde{p}_1 - \tilde{p}_2 = \delta_0$.

Power Calculations

A large sample approximation may be used that is most accurate when the values of n_1 and n_2 are large. The large approximation is made by replacing the values of \hat{p}_1 and \hat{p}_2 in the z-statistic with the corresponding values of p_1 and p_2 under the alternative hypothesis, and then computing the results based on the normal distribution.

Note that in this case, exact calculations are not possible.

Example 1 – Finding Power

Two competing physical therapy treatments have been available for several years but have not yet been compared as to their effectiveness. The comparison of the two treatments is complicated by the sampling method that will be used. Instead of randomly assigning individuals to treatments, the researchers will randomly select two groups of physical therapists. The first group will be selected from those who use treatment 1. The second group will be selected from those who use treatment 2. The researchers will then follow up on the success or failure of the treatment for multiple patients of each physical therapist. The success rate of treatment 2 is known to be about 0.44. The researchers want to examine the effect of the number of physical therapists used in each group and the number of patients for each physical therapist on the power of the test. They wish to determine the power if the treatments are at least 0.07 apart in proportion. They plan to use the Unpooled Z-Test to analyze the data. Based on similar studies, the intracluster correlation is estimated to be 0.02.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 1** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For	Power
Alternative Hypothesis	Two-Sided (H1: P1 - P2 ≠ 0)
Test Type	Z-Test (Unpooled)
Alpha	0.05
K1 (Clusters in Group 1)	10 to 25 by 5
M1 (Average Cluster Size)	10 to 50 by 10
K2 (Clusters in Group 2)	K1
M2 (Average Cluster Size)	M1
Input Type	Differences
D1 (Difference H1 = P1 - P2)	0.07
P2 (Group 2 Proportion)	0.44
ICC (Intracluster Correlation)	0.02

Plots Tab

2D Plot: X (Horizontal) Axis Parameter	K1
3D Plot: X (Horizontal) Axis Parameter	K1

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Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Reports

Numeric Results for Testing Two Proportions (Cluster-Randomized)

Solve For: **Power**
 Groups: 1 = Treatment, 2 = Control
 Test Statistic: Z-Test (Unpooled)
 Hypotheses: H0: P1 - P2 = 0 vs. H1: P1 - P2 ≠ 0

Power	Number of Clusters			Cluster Size		Sample Size			Proportion		Difference D1	Intracluster Correlation ICC	Alpha
	K1	K2	K	M1	M2	N1	N2	N	P1	P2			
0.14998	10	10	20	10	10	100	100	200	0.51	0.44	0.07	0.02	0.05
0.22330	10	10	20	20	20	200	200	400	0.51	0.44	0.07	0.02	0.05
0.27777	10	10	20	30	30	300	300	600	0.51	0.44	0.07	0.02	0.05
0.31930	10	10	20	40	40	400	400	800	0.51	0.44	0.07	0.02	0.05
0.35181	10	10	20	50	50	500	500	1000	0.51	0.44	0.07	0.02	0.05
0.20158	15	15	30	10	10	150	150	300	0.51	0.44	0.07	0.02	0.05
0.31063	15	15	30	20	20	300	300	600	0.51	0.44	0.07	0.02	0.05
0.38870	15	15	30	30	30	450	450	900	0.51	0.44	0.07	0.02	0.05
0.44611	15	15	30	40	40	600	600	1200	0.51	0.44	0.07	0.02	0.05
0.48963	15	15	30	50	50	750	750	1500	0.51	0.44	0.07	0.02	0.05
0.25316	20	20	40	10	10	200	200	400	0.51	0.44	0.07	0.02	0.05
0.39437	20	20	40	20	20	400	400	800	0.51	0.44	0.07	0.02	0.05
0.49061	20	20	40	30	30	600	600	1200	0.51	0.44	0.07	0.02	0.05
0.55827	20	20	40	40	40	800	800	1600	0.51	0.44	0.07	0.02	0.05
0.60761	20	20	40	50	50	1000	1000	2000	0.51	0.44	0.07	0.02	0.05
0.30407	25	25	50	10	10	250	250	500	0.51	0.44	0.07	0.02	0.05
0.47271	25	25	50	20	20	500	500	1000	0.51	0.44	0.07	0.02	0.05
0.58119	25	25	50	30	30	750	750	1500	0.51	0.44	0.07	0.02	0.05
0.65365	25	25	50	40	40	1000	1000	2000	0.51	0.44	0.07	0.02	0.05
0.70424	25	25	50	50	50	1250	1250	2500	0.51	0.44	0.07	0.02	0.05

Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
 K1, K2, and K The number of clusters in groups 1, 2, and both, respectively.
 M1 and M2 The average number of items (subjects) per cluster in groups 1 and 2, respectively.
 N1, N2, and N The sample size (number of subjects) in groups 1, 2, and both, respectively.
 P1 The proportion for group 1 (the treatment group) assuming the alternative hypothesis (H1).
 P2 The proportion for group 2, the standard, reference, baseline, or control group.
 D1 The difference assuming the alternative hypothesis (H1) at which power is calculated. D1 = P1 - P2.
 ICC The intracluster correlation.
 Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A parallel two-group cluster-randomized design will be used to test whether the Group 1 (treatment) proportion (P1) is different from the Group 2 (control) proportion (P2) (H0: P1 - P2 = 0 versus H1: P1 - P2 ≠ 0). The comparison will be made using a two-sided Z-Test (Unpooled) based on the proportion difference, with a Type I error rate (α) of 0.05. The control group proportion (P2) is assumed to be 0.44. The intracluster correlation is assumed to be 0.02. To detect a proportion difference (P1 - P2) of 0.07 (or P1 of 0.51), with 10 clusters of 10 subjects per cluster in Group 1 and 10 clusters of 10 subjects per cluster in Group 2, the power is 0.14998.

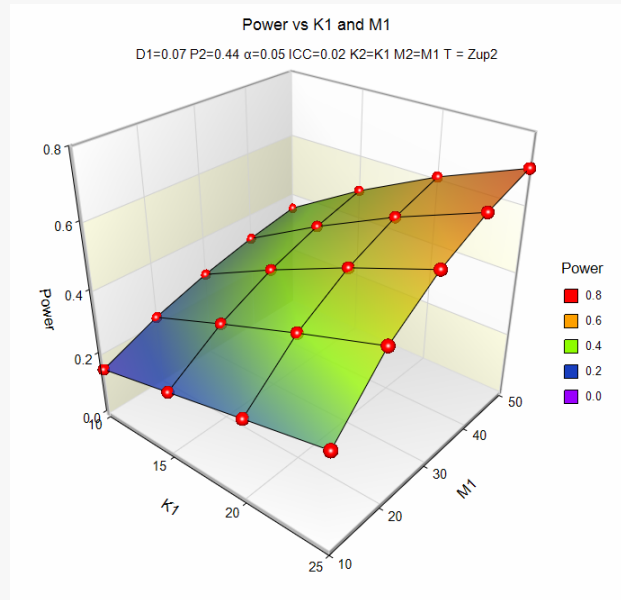
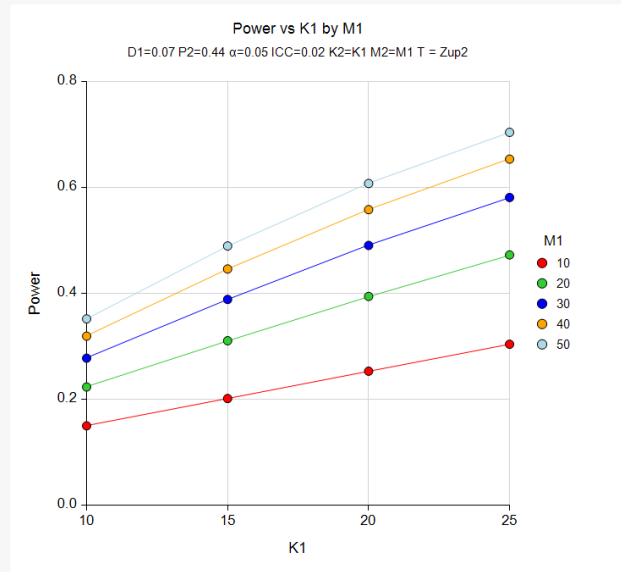
References

Donner, A. and Klar, N. 2000. Design and Analysis of Cluster Randomization Trials in Health Research. Arnold. London.

This report shows the values of each of the parameters, one scenario per row. The values from this table are plotted in the plot below.

Plots Section

Plots



The values from the table are displayed on the above plots. These plots give a quick look at the power that is achieved for various combinations of cluster size and numbers of clusters.

Example 2 – Finding Sample Size

Continuing with Example 1, the maximum number of therapists the researchers hope to use is 25 for each treatment. They decide to determine how many patients each therapist would have to treat to achieve 90% power if the maximum number of therapists is used.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 2** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab	
Solve For	Sample Size (M1)
Alternative Hypothesis	Two-Sided (H1: P1 - P2 ≠ 0)
Test Type	Z-Test (Unpooled)
Power	0.90
Alpha	0.05
K1 (Clusters in Group 1)	25
K2 (Clusters in Group 2)	K1
M2 (Average Cluster Size)	M1
Input Type	Differences
D1 (Difference H1 = P1 - P2)	0.07
P2 (Group 2 Proportion)	0.44
ICC (Intracluster Correlation)	0.02

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results for Testing Two Proportions (Cluster-Randomized)													
Solve For: Sample Size (M1)													
Groups: 1 = Treatment, 2 = Control													
Test Statistic: Z-Test (Unpooled)													
Hypotheses: H0: P1 - P2 = 0 vs. H1: P1 - P2 ≠ 0													
Power	Number of Clusters			Cluster Size		Sample Size			Proportion		Difference D1	Intracluster Correlation ICC	Alpha
	K1	K2	K	M1	M2	N1	N2	N	P1	P2			
0.90004	25	25	50	281	281	7025	7025	14050	0.51	0.44	0.07	0.02	0.05

To achieve 90% power, each therapist would need to be evaluated on 281 patients.

Example 3 – Investigating the Impact of the Intracluster Correlation

Continuing with the scenario given in Example 2, the researchers now want to investigate the required number of therapists if each treats 300 patients and also look at the effect of the intracluster correlation on the sample size. They decide to vary ICC between 0.01 and 0.03 to look at the effect.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 3** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For **Sample Size (K1)**
 Alternative Hypothesis **Two-Sided (H1: P1 - P2 ≠ 0)**
 Test Type **Z-Test (Unpooled)**
 Power **0.90**
 Alpha **0.05**
 M1 (Average Cluster Size) **300**
 K2 (Clusters in Group 2) **K1**
 M2 (Average Cluster Size) **M1**
 Input Type **Differences**
 D1 (Difference|H1 = P1 - P2) **0.07**
 P2 (Group 2 Proportion) **0.44**
 ICC (Intracluster Correlation) **0.01 to 0.03 by 0.005**

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results for Testing Two Proportions (Cluster-Randomized)

Solve For: **Sample Size (K1)**
 Groups: 1 = Treatment, 2 = Control
 Test Statistic: Z-Test (Unpooled)
 Hypotheses: H0: P1 - P2 = 0 vs. H1: P1 - P2 ≠ 0

Power	Number of Clusters			Cluster Size		Sample Size			Proportion		Difference D1	Intracluster Correlation ICC	Alpha
	K1	K2	K	M1	M2	N1	N2	N	P1	P2			
0.91574	15	15	30	300	300	4500	4500	9000	0.51	0.44	0.07	0.010	0.05
0.90764	20	20	40	300	300	6000	6000	12000	0.51	0.44	0.07	0.015	0.05
0.90270	25	25	50	300	300	7500	7500	15000	0.51	0.44	0.07	0.020	0.05
0.90850	31	31	62	300	300	9300	9300	18600	0.51	0.44	0.07	0.025	0.05
0.90496	36	36	72	300	300	10800	10800	21600	0.51	0.44	0.07	0.030	0.05

This report shows that the required number of therapists doubles when the ICC changes from 0.01 to 0.03.

Example 4 – Validation using Donner and Klar (2000)

Donner and Klar (2000), page 63, presents a sample size study in which $P_2 = 0.06$, $D_1 = -0.02$, $D_0=0$, $ICC = 0.01$, $M_1=M_2=100$, two-sided $\alpha = 0.05$, and $\beta = 0.20$. Using the pooled z test statistic, they found the number of subjects to be 3698 in each group, which they round off to 38 clusters per group.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 4** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab	
Solve For	Sample Size (K1)
Alternative Hypothesis	Two-Sided (H1: P1 - P2 ≠ 0)
Test Type.....	Z-Test (Pooled)
Power.....	0.80
Alpha.....	0.05
M1 (Average Cluster Size).....	100
K2 (Clusters in Group 2)	K1
M2 (Average Cluster Size).....	M1
Input Type.....	Differences
D1 (Difference H1 = P1 - P2).....	-0.02
P2 (Group 2 Proportion).....	0.06
ICC (Intracluster Correlation).....	0.01

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results for Testing Two Proportions (Cluster-Randomized)													
Solve For:	Sample Size (K1)												
Groups:	1 = Treatment, 2 = Control												
Test Statistic:	Z-Test (Pooled)												
Hypotheses:	H0: P1 - P2 = 0 vs. H1: P1 - P2 ≠ 0												
Power	Number of Clusters			Cluster Size		Sample Size			Proportion		Difference D1	Intracluster Correlation ICC	Alpha
	K1	K2	K	M1	M2	N1	N2	N	P1	P2			
0.80962	38	38	76	100	100	3800	3800	7600	0.04	0.06	-0.02	0.01	0.05

PASS has also found the required sample size to be 38 clusters.